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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,149	01/23/2007	David N. Watkins	JHU2050-1	5576

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EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
11/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/576,149	WATKINS ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-17 and 19-60* is/are pending in the application.

4a) Of the above claim(s) *24-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-17 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/9/09 has been entered.

Claims 1-5, 7-17 and 19-60 are pending.

Claims 24-60 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 1-5, 7-17 and 19-23 are currently under consideration.

The rejection of claims 1-5, 7, 13-17 and 19 under 35 U.S.C. 102(b) as being anticipated by Watkins et al Nature vol. 422 p. 313 (3/20/03) as evidenced by Zhang et al Bioorganic and Medicinal Chemistry Letters vol. 18 p. 1359 (2008) is withdrawn in view of the new priority date and in view of the Katz declaration filed 3/2/09.

Response to Arguments

Priority

In view of applicant's amendment all claims except for claims 10-11 and 20-21 are granted priority to 10/20/03. Claims 10-11 and 20-21 still have priority to 10/20/04 because as stated in the previous actions the limitations of these claims are mentioned in the provisional application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-5, 7, 13-17, 19-20 and 23 remain rejected under 35 U.S.C. 102(e) as being anticipated by Dudek et al US 2004/0060568 (filed 10/13/00). The reasons for this rejection are of record in the paper mailed 4/9/09. Please note: claims 8-9 are removed from this rejection in view of applicant's arguments.

Applicant again argues that the reference provides no data and that Table 2 merely shows that 3/6 SCLC samples exhibit Gli-1 expression. The reference clearly

provides data to show that Gli-1 is overexpressed in small cell lung carcinoma (table 2) and the reference shows in Example 3 that cyclopamine is a hedgehog antagonist. In fact, the reference shows this for several types of tissues such as breast, lung and prostate. And the reference goes even further to show that hedgehog antagonists (antibody) can be used to inhibit prostate tumor cells (example 6). Drawing an analogy between table 2 and Example 6 it is clear that prostate cancer which over expresses Gli-1 can be treated with hedgehog antagonists, one skilled in the art would immediately envisage the same for small cell lung carcinoma.

Claims 1-5, 8-17 and 20-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Ling et al US 2005/0054568 (8/23/03). The reasons for this rejection are of record in the paper mailed 4/9/09.

Applicant again argues that the reference provides no data and that table 2 merely teaches that 7/11 lung cancers exhibit Gli-1 expression. The reference clearly provides data to show that Gli-1 is overexpressed in small cell lung carcinoma (table 2) and the reference shows in Example 3 that cyclopamine is a hedgehog antagonist. In fact, the reference shows this for several types of tissues such as breast, lung and prostate. And the reference goes even further to show that hedgehog antagonists (antibody) can be used to inhibit prostate tumor cells (example 12). Drawing an analogy between table 2 and Example 12 it is clear that prostate cancer which over expresses Gli-1 can be treated with hedgehog antagonists, one skilled in the art would immediately envisage the same for small cell lung carcinoma.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5, 7, 13-17, 19 and 23 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43-75 of copending Application No. 11/338503. The reasons for this rejection are of record in the paper mailed 10/31/08.

The terminal disclaimer filed 9/9/09 is not approved because the Attorney's registration number and signature do not match.

Claims 1-5, 7, 13-17, 19 and 23 remain directed to an invention not patentably distinct from claims 43-75 of commonly assigned 11/338503. . The reasons for this rejection are of record in the paper mailed 10/31/08.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-9, 11-17, 19-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dudek et al US 2004/0060568 (filed 10/13/00) in view of Chen et al

PNAS vol. 99 p. 14071 (10/29/2002). This rejection is re-written in view of applicant's amendment.

Dudek et al has been discussed above.

The only difference between the instant invention and the reference is the use of KAAD-cyclopamine and the combination use of an antagonist with an anti-Hh antibody.

Chen et al disclose that that KAAD-cyclopamine is a potent cyclopamine derivative that is more potent in inhibiting hedgehog activity (page 14072, bottom of first column).

Thus, in view of Chen et al and the disclosure that KAAD-cyclopamine is more effective than cyclopamine, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use KAAD-cyclopamine in place of cyclopamine to inhibit small cell lung carcinoma. The combination of the antagonist with the antibody is obvious because Dudek discloses that anti-hH antiboies are effective hedgehog antagonists, and "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to applicant's arguments

Applicant argues that Chen fails to overcome the deficiencies of Dudek et al. As discussed above, it is the Examiner's position that Dudek et al has no deficiencies.

Applicant argues that the action provides no rational for combining the references. As stated in the rejection, Chen et al disclose that KAAD-cyclopamine is more effective than cyclopamine thus here is the rational for using KAAD-cyclopamine instead on cyclopamine.

Applicant argues that neither Dudek et al or Chen et al teach the use of antibodies or fragments thereof to reduce, inhibit or ameliorate SCLC. AS stated in the rejection, Applicant is directed to paragraphs [0489] and [0502] of Dudek et al.

Claims 1-5, 8-17 and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ling et al US 2005/0054568 (8/23/03) in view of Chen et al PNAS vol. 99 p. 14071 (10/29/2002). This rejection is re-written in view of applicant's amendment.

Ling et al has been discussed above.

The only difference between the instant invention and the reference is the use of KAAD-cyclopamine and the combination use of an antagonist with an anti-Hh antibody.

Chen et al disclose that KAAD-cyclopamine is a potent cyclopamine derivative that is more potent in inhibiting hedgehog activity (page 14072, bottom of first column).

Thus, in view of Chen et al and the disclosure that KAAD-cyclopamine is more effective than cyclopamine, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use KAAD-cyclopamine in place of cyclopamine to inhibit small cell lung carcinoma. The combination of the antagonist with the antibody is obvious because Ling discloses that anti-hH antiboies are effective hedgehog

antagonists, and "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to applicant's arguments

Applicant argues that Chen fails to overcome the deficiencies of Ling et al. As discussed above, it is the Examiner's position that Ling et al has no deficiencies.

Applicant argues that the action provides no rational for combining the references. As stated in the rejection, Chen et al disclose that KAAD-cyclopamine is more effective than cyclopamine thus here is the rational for using KAAD-cyclopamine instead on cyclopamine.

Applicant argues that neither Ling et al or Chen et al teach the use of antibodies or fragments thereof to reduce, inhibit or ameliorate SCLC. As stated in the rejection, Applicant is directed to the entire reference of Ling et al.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued

examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Monday-Thursday 6am to 2pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/
Primary Examiner
Art Unit 1643

sjh